

Researchers Under Criminal Investigation For VA Drug Study Deaths in New York

By M. Alexander Otto

Two medical researchers are under criminal investigation for the deaths of at least five patients in drug studies at the Stratton Veterans Affairs Medical Center in Albany, N.Y., BNA has learned, as VA officials take action to address study safety issues the incidents have uncovered.

Dr. James Holland, former chief of oncology at the Albany center, and Paul Kornak, former research assistant in the hematology and oncology department, could face involuntary manslaughter charges if federal investigators determine they were at fault in the deaths of patients enrolled in the studies, sources close to the case said.

Either Holland or Kornak or both allegedly fabricated data, improperly enrolled patients, failed to report adverse events, altered medical charts, and committed other serious acts of research misconduct in drug company studies involving almost 100 patients. The actions probably caused one death and may have caused at least four more, according to Stratton's preliminary investigation.

Veterans Affairs spokesman John Wooditch confirmed the criminal investigations.

The Albany center dismissed Holland in early January and Kornak on Jan. 31, Arthur K. Wu, staff director of the House Veterans' Affairs Subcommittee on Oversight and Investigations, told BNA Feb. 3.

Some of the patients signed up for the pair's studies allegedly were not appropriate candidates for the experimental drugs given. Taking them could have at least contributed to patients' deaths, said Wu, who helps advise the House Committee on Veterans' Affairs on VA research issues.

The Albany center released a press statement Feb. 4 admitting the misconduct probe. A VA press officer acknowledged the move was a response to BNA's investigation and breaking of the story that morning.

"The medical center has taken the necessary steps to ensure that all ongoing research studies strictly adhere to regulations and procedures, and that the interests of all study participants are protected," according to the Feb. 4 statement, which gave few details. Albany had declined to talk to BNA previously.

Link to Drug Companies.

VA medical centers conduct a vast amount of medical research involving veterans. As at university medical centers, a great many of those studies are funded by the pharmaceutical industry.

Financial ties between drug companies and researchers increasingly have been called into question by regulators who suspect the ties encourage some researchers to fabricate data and take other steps to help companies get new products approved by the Food and Drug Administration (*see related item in the News section*).

Typically, each patient enrolled in a trial earns an investigator \$1,000 or more in recruitment fees. Holland was paid by drug firms to enroll patients, but Wu was uncertain of the amount.

Researchers "may be too incentivized to recruit patients. They may be too incentivized to get results," he said.

A string of research deaths and other mishaps in recent years have put medical researchers under fire from patient advocates and others. The VA anticipates significant coverage when the Albany deaths break in the general interest media.

Holland and Kornak could not be reached for comment.

Nationwide Research Review.

The problems were first uncovered about a year ago by staff at Ilex Oncology Inc. of San Antonio who noticed discrepancies in data submitted by Holland and Kornak. The pair had been studying Ilex's experimental bladder cancer drug, eflornithine, in four Stratton patients.

The Albany study was part of a nationwide trial involving 450 patients funded by Ilex and the National Cancer Institute. The drug, also known as DFMO, is being studied for several cancer uses and long has been used to treat tropical parasite infections.

The discrepancies triggered an internal investigation by Albany. Federal investigators from the VA and from the U.S. attorney's office started looking into the matter in the fall.

FDA found substantial problems in 54 of the 55 patient charts prepared by Holland and Kornak that it reviewed during its own early-January investigation. Federal authorities have confirmed Stratton's original conclusions.

Ilex originally refused to talk to BNA about the Albany investigations, but after the story broke Feb. 4 spokesman Barry Cohen explained that "Ilex continues to cooperate with the investigation" and that the company "has been advised that it is not a target of the investigation."

Ilex excluded the Albany data and shut down its DFMO study there when problems emerged, he noted. Cohen said he was unsure whether the compound was studied at other VA centers.

Federal law enforcement workers are reviewing "the entire universe of research touched by" Holland and Kornak, Wu said. Albany also has reviewed all of its studies "with a microscope," he explained.

A nationwide review of how research is conducted at VA medical centers could follow the Albany investigation; VA investigators have been convicted of criminal research misconduct in the past, Wu said. But he was quick to note that the kinds of problems suspected at Albany have occurred in non-VA research programs as well.

Washington Fallout.

The situation already has had political consequences at the VA's Washington, D.C., headquarters.

In mid-January, VA Under Secretary for Health Dr. Robert Roswell announced that the office that polices the safety of patients in VA studies had been abolished for failing to inform VA administrators quickly enough about the Albany deaths, Wu said.

Roswell planned to put the VA office that funds and promotes research in charge of study safety, a scheme prominent researchers told BNA was unworkable. At times, measures to protect patients can delay or even derail trials.

Dr. Greg Koski, who until his resignation in November 2002 oversaw patient safety in the thousands of human studies funded each year by the National Institutes of Health, told BNA the abolition of the office was a "big step backward" in patient protections.

A VA research safety officer at a Northeast VA center said she was "shocked" by the suddenness of the move and the fact that there was no official announcement. "This is not good and we are not happy about it," she said, noting that the office had a reputation for "handling things fairly."

Rep. Steve Buyer (R-Ind.), a House Committee on Veterans' Affairs member, shelved the move in a Jan. 27 letter obtained by BNA, and asked VA Secretary Anthony J. Principi to reconsider and further justify the plan.

The body, known officially as the Office of Research Compliance and Assurance, was established in 1999 as an independent watchdog office within the VA specifically to allow it the freedom to enforce human research protection rules.

"To get rid of ORCA" because it should have detected the Albany deaths earlier "is ludicrous," Wu said. He noted that no enforcement agency can prevent an individual from deciding to do something criminal.

Several observers suspected ORCA was "taking the fall" for the deaths, and noted that there long has been resentment among some VA research administrators against an independent body to police study safety.

In the past, ORCA has halted research at centers it thought were not adequately protecting research subjects.

A Jan. 30 subcommittee meeting revealed that ORCA may well have kept VA staff informed of the Albany situation, Wu said. Roswell has since told BNA the abolition of ORCA no longer was a "done deal," but would not elaborate.

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